selected from SEQ ID NOs: 3, 5, 7, 9, 11, 13, 15, 16, 17, 20, 22-24, 26-28, 30-35, 37-40, 42-43, 45 or 47.

50. The isolated nucleic acid molecule of claim 9 wherein said protein modulates cytokine-mediated signal transduction by inhibiting the activity of JAK kinases.

51. The isolated nucleic acid molecule of claim 9 wherein said protein modulates cytokine-mediated signal transduction by reducing the phosphorylation of cell receptors and STATs.

REMARKS

In the Office Action dated February 24, 2000, claims 1-15 are under consideration. Claims 16-40 have been withdrawn from consideration. In response to the objections and rejections set forth in the Office Action, Applicants have amended the specification and the claims. More specifically, Applicants have canceled claims 1-5 and 13-40 without prejudice, amended claims 6-12, and added claims 41-51. Applicants reserve the right to pursue the subject matter of the canceled claims by filing one or more continuing applications. The foregoing amendment, when considered in view of the following remarks, is deemed to place the application in condition for allowance. No new matter has been introduced. Favorable consideration of all pending claims is respectfully requested.

As set forth in the Office Action, the specification is objected to for certain informalities in the Brief Description of

Drawings. More specifically, the Examiner indicates that there is no description for Figure 17; and the descriptions of Figures 19, 22, 25, 28, 30, 33, 37-38, 41, 44 and 46 are incomplete.

In response, Applicants have amended the specification by adding a description for Figure 17, and the allegedly missing information in the descriptions of Figures 19, 22, 25, 28, 30, 33, 37-38, 41, 44 and 46. Support for the description of Figure 17 is found in the specification, e.g., at page 80. Support for the amendment to the descriptions of Figures 19, 22, 25, 28, 30, 33, 37-38, 41, 44 and 46 is found throughout the specification and in the corresponding drawings submitted with the application. Accordingly, the objection to the specification is obviated and withdrawal thereof is respectfully requested.

Applicants further submit that the specification has also been amended to correct an error to the description of the SOCS box motif in the specification. More specifically, the SOCS box motif is described in the specification as comprising the sequence:

$$X_1X_2X_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}X_{14}X_{15}X_{16}[X_i]_nX_{17}X_{18}X_{19}X_{20}$$

$$X_{21}X_{22}X_{23}[X_j]_nX_{24}X_{25}X_{26}X_{27}X_{28}$$

wherein $[X_j]_n$ is a sequence of n amino acids wherein n is from 1 to 50 amino acids and wherein the sequence Xj may comprise the same or different amino acids selected from any amino acid residue. It is respectfully submitted that the delineation of n as "from 1 to 50" was an inadvertent typographical error, and has been corrected to recite "from 0 to 50". This amendment is

supported by the specification. For example, the SOCS box of mSOCS-3 (SEQ ID NO:54) comprises the sequence of VATLQHLCRKTVNGHLDSYEKVTQLPGPIREFL, wherein X_1-X_{16} is VATLQHLCRKTVNGHL, [Xi]n is DSYEK, X_{17}-X_{23} is VTQLPGP, [Xj]n is no amino acid (i.e., n=0), and X_{24}-X_{28} is IREFL. Accordingly, Applicants submit that the correction of n as in [Xj]n from the recitation "1 to 50" to the recitation "0 to 50" does not introduce new matter.

Applicants respectfully submit that the specification has also been amended to replace the Sequence Listing of record with a substitute Sequence Listing. Applicants provide herewith a substitute paper copy and a substitute computer-readable copy of such Sequence Listing, along with a Verification Under 37 C.F.R. §1.821(f), stating that these copies are identical.

In the substitute Sequence Listing, Applicants have added SEQ ID NOS: 51-68. SEQ ID NO: 51 represents the consensus sequence of the SOCS box, which is described in the specification and original claim 6, for example. SEQ ID NOS: 52-68 represent the SOCS boxes found in specific SOCS proteins described in the application. Support for SEQ ID NOS: 52-68 is found in the specification, for example, in the Sequence Listing included in the application as originally filed (pages 107-182), Table 1 (pages 17-18), Figure 13 and claim 6. For the Examiner's convenience, Applicants have provided herewith a table (attached as Exhibit A) which illustrates the sequences of SEQ ID NOS: 52-68, the relationship of such SOCS box sequences to the SOCS

proteins, and appropriate supporting references in the specification. Applicants respectfully submit that SEQ ID NOS: 51-68 do not introduce new matter.

As further set forth in the Office Action, claims 6-12 are objected to as allegedly written in improper form. The Examiner indicates that claim 6, written as a multiple dependent claim, can not depend from claim 4 which is another multiple dependent claim.

Applicants submit that claim 6 as presently amended is an independent claim. Accordingly, the objection to claims 6-12 is overcome and withdrawal thereof is respectfully requested.

Claims 1-6 and 13-15 are rejected under 35 U.S.C. §101 as allegedly directed to non-statutory matter.

Claims 1-5 and 13-15 have been canceled without prejudice, thus rendering the rejection of these claims moot. Claim 6 has been amended to recite an isolated nucleic acid molecule. It is submitted that the rejection under 35 U.S.C. §101 is overcome and withdrawal thereof is respectfully requested.

Claims 1-5 and 13-15 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claims 1-5 and 13-14 are further rejected under 35 U.S.C. §112, first paragraph.

Applicants submit that these rejections are moot in view of the cancellation of claims 1-5 and 13-15. Thus, withdrawal of the rejections under 35 U.S.C. §112, first and second paragraphs, is respectfully requested.

Claims 13 and 14 are rejected under §102(b) as allegedly anticipated by Watson et al. (Molecular Biology of the Gene, 4th edition). Watson et al. teach nucleic acids encoding individual amino acids. The Examiner has pointed out that the rejection is directed to the recitation of the claims "having at least 15% similarity to all or part of the listed sequences" (emphasis added).

It is respectfully submitted that the rejection is moot in view of the cancellation of claims 13-14. Thus, withdrawal thereof is requested.

Claim 13 is rejected under §102(e) as allegedly anticipated by Smith et al. (U.S. Patent 5,871,960). The Examiner contends that Smith et al. teach a nucleic acid sequence that has 45% sequence similarity to a nucleic acid encoding SEQ ID NO:4. The Examiner has pointed out that the rejection is directed to the recitation of the claims "having at least 15% similarity to all or part of the listed sequences".

It is respectfully submitted that the rejection is moot in view of the cancellation of claim 13. Thus, withdrawal thereof is requested.

Claim 14 is rejected under §102(b) as allegedly anticipated by Schaffer et al. (WO94/28156, Dec. 8, 1994). The Examiner contends that Schaffer et al. teach a nucleic acid sequence, designated as accession number Q76213, that shares 46% local similarity with Applicants' SEQ ID NO:3. The Examiner has pointed out that the rejection is directed to the recitation of

the claims "having at least 15% similarity to all or part of the listed sequences".

It is respectfully submitted that the rejection is moot in view of the cancellation of claim 14. Thus, withdrawal thereof is requested.

It is further submitted that claims 41-48 have been added which are fully supported by the specification.

More specifically, added claim 41 is supported by the specification and original claim 6. X_1 in added claim 41 can be L, I, V, M or P, whereas X_1 in claim 6 is L, I, V, M, A or P.

Added claim 42 is drawn to an isolated nucleic acid molecule encoding a protein comprising any one of SEQ ID NOS: 52-68, i.e., the specific SOCS motifs found in the SOCS proteins described in the specification. As submitted above, support for SEQ ID NOs: 52-66 is found in the specification.

Added claim 43 is drawn to an isolated nucleic acid molecule encoding a protein comprising a sequence, which sequence has 70% similarity to any one of SEQ ID NOS: 52-68. Support for claim 43 can be found throughout the specification, for example, at page 43, and by original claims 6 and 13.

Added claim 44 is supported by original claims 1-5 and 15.

Added claims 45-46 are drawn to nucleic acid molecules encoding a protein having at least about 50% similarity to any one of the specific SEQ ID NOs recited therein. Support for

claim 45-46 can be found throughout the specification, for example, at page 43.

Added claims 47-49 are drawn to isolated nucleic acid molecules comprising any one of the SEQ ID NOs recited therein, sequences which hybridize under low stringency conditions to any one of the SEQ ID NOs recited therein, or sequences which have 50% similarity to any one of the SEQ ID NOs recited therein. Support for claims 47-49 can be found in the specification, e.g., at pages 37 and 43.

Added claims 50-51 depend from claim 9 and delineate the manner by which the proteins encoded by the claimed nucleic acid molecules regulate cytokine-mediated signal transduction. Support for claims 50-51 can be found in the specification, e.g., at pages 71-75 (Examples 13-16).

Applicants further submit that the nucleic acid molecules of added claims 41-51 are not taught anywhere in Watson et al., Smith et al., or Schaffer et al.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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